

What Is Claimed Is:

1. A panel of expression cassettes, comprising  
a first expression cassette comprising a first control element derived from a first stress-inducible gene, said control element operable linked to sequences encoding a first light generating polypeptide, and  
a second expression cassette comprising a second control element derived from a second stress-inducible gene, said second control element operable linked to sequences encoding a second light generating polypeptide.
2. The panel of claim 1, said panel further comprising  
a third expression cassette comprising a control element derived from a third stress-inducible gene, said third control element operable linked to sequences encoding a third light generating polypeptide.
3. The panel of claim 2, wherein (i) said first, second, and third control elements are each derived from a different gene, and (ii) said first, second, and third light generating polypeptides produce the same color of light.
4. The panel of claim 2, wherein (i) said first, second, and third control elements are each derived from a different gene, and (ii) at least two of said first, second, and third light generating polypeptides produce different colors of light.
5. The panel of claim 2, said panel further comprising additional expression cassettes, wherein each expression cassette comprises a control element derived from a different stress-inducible gene, said control element operable linked to sequences encoding a light generating polypeptide.
6. A panel of expression cassettes, comprising

a first expression cassette comprising a first control element derived from an first apoptosis-related gene, said control element operable linked to sequences encoding a first light generating polypeptide, and

a second expression cassette comprising a second control element derived from an second apoptosis-related gene, said second control element operable linked to sequences encoding a second light generating polypeptide.

7. The panel of claim 6, said panel further comprising

a third expression cassette comprising a control element derived from an third apoptosis-related gene, said third control element operable linked to sequences encoding a third light generating polypeptide.

8. The panel of claim 7, wherein (i) said first, second, and third control elements are each derived from a different gene, and (ii) said first, second, and third light generating polypeptides produce the same color of light.

9. The panel of claim 7, wherein (i) said first, second, and third control elements are each derived from a different gene, and (ii) at least two of said first, second, and third light generating polypeptides produce different colors of light.

10. The panel of claim 7, said panel further comprising additional expression cassettes, wherein each expression cassette comprises a control element derived from a different apoptosis-related gene, said control element operable linked to sequences encoding a light generating polypeptide.

11. A panel of expression cassettes, comprising

a first expression cassette comprising a first control element derived from a first angiogenesis-related gene, said control element operable linked to sequences encoding a first light generating polypeptide, and

a second expression cassette comprising a second control element derived from a second angiogenesis-related gene, said second control element operable linked to sequences encoding a second light generating polypeptide.

12. The panel of claim 11, said panel further comprising  
a third expression cassette comprising a control element derived from a third angiogenesis-related gene, said third control element operable linked to sequences encoding a third light generating polypeptide.

13. The panel of claim 12, wherein (i) said first, second, and third control elements are each derived from a different gene, and (ii) said first, second, and third light generating polypeptides produce the same color of light.

14. The panel of claim 12, wherein (i) said first, second, and third control elements are each derived from a different gene, and (ii) at least two of said first, second, and third light generating polypeptides produce different colors of light.

15. The panel of claim 12, said panel further comprising additional expression cassettes, wherein each expression cassette comprises a control element derived from a different angiogenesis-related gene, said control element operable linked to sequences encoding a light generating polypeptide.

16. A panel of expression cassettes, comprising  
a first expression cassette comprising a first control element derived from a first development-related gene, said control element operable linked to sequences encoding a first light generating polypeptide, and  
a second expression cassette comprising a second control element derived from a second development-related gene, said second control element operable linked to sequences encoding a second light generating polypeptide.

17. The panel of claim 16, said panel further comprising  
a third expression cassette comprising a control element derived from a third  
development-related gene, said third control element operable linked to sequences encoding a  
third light generating polypeptide.

18. The panel of claim 17, wherein (i) said first, second, and third control elements are  
each derived from a different gene, and (ii) said first, second, and third light generating  
polypeptides produce the same color of light.

19. The panel of claim 17, wherein (i) said first, second, and third control elements are  
each derived from a different gene, and (ii) at least two of said first, second, and third light  
generating polypeptides produce different colors of light.

20. The panel of claim 17, said panel further comprising additional expression cassettes,  
wherein each expression cassette comprises a control element derived from a different  
development-related gene, said control element operable linked to sequences encoding a light  
generating polypeptide.

21. A panel of expression cassettes, comprising  
a first expression cassette comprising a first control element derived from a first  
oncogenesis-related gene, said control element operable linked to sequences encoding a first  
light generating polypeptide, and  
a second expression cassette comprising a second control element derived from a second  
oncogenesis-related gene, said second control element operable linked to sequences encoding a  
second light generating polypeptide.

22. The panel of claim 21, said panel further comprising  
a third expression cassette comprising a control element derived from a third  
oncogenesis-related gene, said third control element operable linked to sequences encoding a  
third light generating polypeptide.

23. The panel of claim 22, wherein (i) said first, second, and third control elements are each derived from a different gene, and (ii) said first, second, and third light generating polypeptides produce the same color of light.

24. The panel of claim 22, wherein (i) said first, second, and third control elements are each derived from a different gene, and (ii) at least two of said first, second, and third light generating polypeptides produce different colors of light.

25. The panel of claim 22, said panel further comprising additional expression cassettes, wherein each expression cassette comprises a control element derived from a different oncogenesis-related gene, said control element operable linked to sequences encoding a light generating polypeptide.

26. A panel of expression cassettes, comprising  
a first expression cassette comprising a first control element derived from a first gene whose expression is induced in a host in response to an infectious agent, said control element operable linked to sequences encoding a first light generating polypeptide, and  
a second expression cassette comprising a second control element derived from a second gene whose expression is induced in a host in response to an infectious agent, said second control element operable linked to sequences encoding a second light generating polypeptide.

27. The panel of claim 26, said panel further comprising  
a third expression cassette comprising a control element derived from a third gene whose expression is induced in a host in response to an infectious agent, said third control element operable linked to sequences encoding a third light generating polypeptide.

28. The panel of claim 27, wherein (i) said first, second, and third control elements are each derived from a different gene, and (ii) said first, second, and third light generating polypeptides produce the same color of light.

29. The panel of claim 27, wherein (i) said first, second, and third control elements are each derived from a different gene, and (ii) at least two of said first, second, and third light generating polypeptides produce different colors of light.

30. The panel of claim 27, said panel further comprising additional expression cassettes, wherein each expression cassette comprises a control element derived from a different gene whose expression is induced in a host in response to an infectious agent, said control element operable linked to sequences encoding a light generating polypeptide.

31. A panel of expression cassettes, comprising  
a first expression cassette comprising a first control element derived from a first inflammation-related gene, said control element operable linked to sequences encoding a first light generating polypeptide, and  
a second expression cassette comprising a second control element derived from a second inflammation-related gene, said second control element operable linked to sequences encoding a second light generating polypeptide.

32. The panel of claim 31, said panel further comprising  
a third expression cassette comprising a control element derived from a third inflammation-related gene, said third control element operable linked to sequences encoding a third light generating polypeptide.

33. The panel of claim 32, wherein (i) said first, second, and third control elements are each derived from a different gene, and (ii) said first, second, and third light generating polypeptides produce the same color of light.

34. The panel of claim 32, wherein (i) said first, second, and third control elements are each derived from a different gene, and (ii) at least two of said first, second, and third light generating polypeptides produce different colors of light.

35. The panel of claim 32, said panel further comprising additional expression cassettes, wherein each expression cassette comprises a control element derived from a different inflammation-related gene, said control element operable linked to sequences encoding a light generating polypeptide.

36. A kit comprising a panel of expression cassettes of claim 1.

37. The kit of claim 36, wherein each of said expression cassettes further comprises a vector suitable for use in generating transgenic, non-human animals.

38. A transgenic, non-human animal comprising a panel of expression cassettes of claim 1, wherein said expression cassettes have been introduced into said animal or an ancestor of said animal, at an embryonic stage.

39. A cohort of transgenic, non-human animals comprising a panel of expression cassettes of claim 1, wherein (i) each transgenic animal of the cohort contains at least one expression cassette of the panel, and (ii) the transgenic animals comprising the cohort are substantially isogenic relative to each other.

40. A method of determining the effect of an analyte on gene expression mediated by selected control elements, wherein said expression is in a non-human living animal, said method comprising

administering the analyte to a living transgenic non-human animal of claim 38, wherein administering of said analyte is carried out under conditions that permit light generation mediated by said light generating polypeptide in the transgenic animal,

determining the effect of the analyte on expression of the light generating polypeptide in a living animal wherein said expression is mediated by at least one of the control elements.

Sub  
B2

41. The method of claim 40, wherein said conditions that permit light generation mediated by the light generating polypeptide includes administering, to the animal, at least one substrate for the light generating polypeptide.

42. A method of determining the effect of an analyte on gene expression mediated by selected control elements, wherein said expression is in a living non-human animal, said method comprising

administering the analyte to each transgenic animal comprising the cohort of claim 39, wherein administering of said analyte is carried out under conditions that permit light generation mediated by said light generating polypeptide in the transgenic animal,

determining the effect of the analyte on expression of the light generating polypeptide in a living animal wherein said expression is mediated by at least one of the control elements.

Sub  
B3

43. The method of claim 40, wherein the expression cassettes of said transgenic animal comprise control elements derived from stress-inducible genes, and said analyte is screened for its affect on expression of stress-inducible genes.

44. The method of claim 42, wherein the expression cassettes of said transgenic animal comprise control elements derived from stress-inducible genes, and said analyte is screened for its affect on expression of stress-inducible genes.

Sub  
B4

45. A noninvasive method for detecting a level expression in response to an analyte, wherein said expression is (i) mediated by selected control elements, and (ii) in a non-human living animal, said method comprising

(a) administering the analyte to a living transgenic non-human animal of claim 38, wherein administering of said analyte is carried out under conditions that permit light generation mediated by said light generating polypeptide,

(b) placing the animal within a detection field of a photo detector device,

(c) maintaining the animal in the detection field of the device, and



Sub  
B4

~~(d) during said maintaining, measuring photon emission from the animal with the photo detector device to detect the level of expression of the light generating polypeptide in the living animal wherein said expression is mediated by at least one of the control elements.~~

46. The method of claim 45, further comprising,

~~(e) repeating steps (b) through (d) at selected intervals, wherein said repeating is effective to detect changes in the level of the light emission in the animal over time.~~

47. A noninvasive method for detecting a level expression in response to an analyte, wherein said expression is (i) mediated by selected control elements, and (ii) in a non-human living animal, said method comprising

(a) administering the analyte to each transgenic animal comprising the cohort of claim 39, wherein administering of said analyte is carried out under conditions that permit light generation mediated by said light generating polypeptide,

(b) placing each animal within a detection field of a photo detector device,

(c) maintaining each animal in the detection field of the device, and

(d) during said maintaining, measuring photon emission from each animal with the photo detector device to detect the level of expression of the light generating polypeptide in a living animal wherein said expression is mediated by at least one of the control elements.

48. The method of claim 47, further comprising,

(e) repeating steps (b) through (d) at selected intervals, wherein said repeating is effective to detect changes in the level of the light emission in each animal over time.

Sub  
B5

~~49. A method of providing a transgenic, non-human animal suitable for screening a selected analyte, comprising~~

~~generating a transgenic animal of claim 38, and~~

~~providing said transgenic animal or progeny thereof for use in screening a selected analyte.~~

50. A method of providing transgenic, non-human animals suitable for screening a selected analyte, comprising  
generating a cohort of transgenic animals of claim 39, and  
providing said cohort of transgenic animals or progeny thereof for use in screening a selected analyte.

51. A method of producing a transgenic, non-human animal, said animal having at least one single-copy, non-essential gene in its genome, comprising  
transfecting a first embryonic stem cell of said animal with a first linear vector comprising  
(a) a first selectable marker and a first expression cassette of claim 1, and  
(b) targeting polynucleotide sequences homologous to a first single-copy, non-essential gene in said animal's genome, said targeting polynucleotide sequences flanking (a), wherein (i) the length of the polynucleotide sequences are sufficient to facilitate homologous recombination between the vector and the first single-copy, non-essential gene, and (ii) said control elements are heterologous to the first single-copy, non-essential gene;  
selecting first embryonic stem cells which each have said first selectable marker and first expression cassette integrated into its genome;  
injecting said first embryonic stem cells into a host embryo,  
implanting said embryo in a foster mother,  
maintaining said foster mother under conditions which allow production of a first offspring that is a transgenic, non-human animal carrying said first expression cassette.

52. The method of claim 51, wherein said first offspring is capable of germline transmission of said first expression cassette.

53. The method of claim 52 further comprising breeding said first offspring with a breeding partner, wherein the breeding partner is substantially isogenic with the first embryonic stem cells, wherein said breeding yields first transgenic F1 offspring carrying said first expression cassette.

54. The method of claim 53, further comprising breeding a first F1 offspring carrying said first expression cassette with another first F1 offspring carrying said first expression cassette, wherein said breeding yields first transgenic F2 offspring carrying said first expression cassette.

55. The method of any of claim 54, wherein said transgenic, non-human animal is a mouse.

56. The method of claim 55, wherein said embryonic stems cells are derived from a mouse having a dark coat color.

57. The method of claim 56, wherein said animal substantially isogenic with the embryonic stem cells has a light coat color.

58. The method of claim 57, wherein said F2 offspring carrying said reporter cassette has a light coat color.

59. The method of claim 58, wherein said embryonic stems cells are derived from a C57BL/6 mouse having a dark coat color, and said animal substantially isogenic with the embryonic stem cells is a C57BL/6-Tyr C2j/+ mouse having a light coat color.

60. The method of claim 51, further comprising  
transfecting a second embryonic stem cell of said animal with a second linear vector comprising

- (a) a second selectable marker and a second expression cassette of claim 1, and
- (b) targeting polynucleotide sequences homologous to a second single-copy, non-essential gene in said animal's genome, said targeting polynucleotide sequences flanking (a), wherein (i) the length of the polynucleotide sequences are sufficient to facilitate homologous

recombination between the vector and the second single-copy, non-essential gene, and (ii) said control elements are heterologous to the second single-copy, non-essential gene;

selecting second embryonic stem cells which each have said second selectable marker and second expression cassette integrated into its genome;

injecting said second embryonic stem cells into a host embryo,

implanting said embryo in a foster mother,

maintaining said foster mother under conditions which allow production of a second offspring that is a transgenic, non-human animal carrying said first expression cassette.

61. The method of claim 60, wherein said second offspring is capable of germline transmission of said second expression cassette.

62. The method of claim 61 further comprising breeding said second offspring with a breeding partner, wherein the breeding partner is substantially isogenic with the second embryonic stem cells, wherein said breeding yields transgenic F1 second offspring carrying said second expression cassette.

63. The method of claim 62, further comprising breeding a second F1 offspring carrying said second expression cassette with another second F1 offspring carrying said second expression cassette, wherein said breeding yields second transgenic F2 offspring carrying said second expression cassette.

64. The method of claim 63 further comprising breeding said first transgenic F2 offspring with said second transgenic F2 offspring to obtain a third transgenic, non-human animal carrying both said first and second expression cassettes.

Add  
A2